

REMARKS

Entry of this Amendment is proper under 37 C.F.R. § 1.116 because the Amendment places the application in condition for allowance for the reasons discussed herein; does not raise any new issue requiring further search and/or consideration, because the amendments amplify issues previously discussed throughout prosecution; does not present any additional claims; and places the application in better form for an appeal should an appeal be necessary. The Amendment is necessary and was not earlier presented because it is made in response to arguments raised in the final rejection and in the interview of May 28, 2003, discussed below. Entry of the Amendment, reexamination and further and favorable consideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.116, are thus respectfully requested.

As correctly stated in the Official Action, Claims 1, 4, and 24-33 are pending in the present application. Claims 1, 4, and 24-33 stand rejected.

By the present amendment, Claims 1 and 4 have been amended. Support for these amendments can be found, at least, on page 2, lines 10-22; page 5, last two lines, to page 6 line 11; and Claims 1 and 5 as originally filed. No new matter has been added.

Interview Summary

Applicants express their gratitude for the courtesy shown by Examiner Kim to Applicants' undersigned representative at the personal interview on May 28, 2003. During the interview, Applicants' representative discussed that the candidate subjects of the

presently claimed invention and of Lee et al. were different. That is, the subjects of Lee et al. are subjects with scar tissue, whereas the subjects of the presently claimed invention require contractile fiber decontraction or relaxation to loosen and/or relax the skin. Examiner Kim suggested amending claim 1 to clarify that the populations treated in Lee et al. and the presently claimed invention were different.

Applicants' representative indicated that the "smoothing of the skin" in Claim 4 resulted from the relaxation or decontraction of the contractile fibers underlying the cutaneous and subcutaneous skin and was not in conflict with the cited publications or the present specification. Examiner Kim suggested amending Claim 4 to explicitly recite this effect.

Applicants' representative and Examiner Kim agreed that the above amendments would overcome the rejection of claim 4 under 35 U.S.C. § 112, second paragraph, and the double patenting rejection.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 4 stands rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Examiner indicates that it is not clear whether Claim 4 further limits Claim 1. The Examiner also asserts that the phrase "smoothing the skin" seems to have an opposite meaning in the art, as shown by Breton et al. (U.S. Patent No. 6,440,433). This rejection, to the extent that it applies to Claim 4 as amended, is respectfully traversed.

Without conceding to the merits of this rejection and solely in an effort to expedite prosecution, Claim 4 has been amended to recite that the "loosening and/or relaxing

of...skin tissue smooths the skin." Moreover, Applicants respectfully point out that the term smoothing is consistent with the specification. That is, the relaxation or decontraction of contractile fibers underlying the cutaneous or subcutaneous skin tissue will result in the skin tissue being less "bunched up" and will smooth the skin. In contrast, the Breton '433 patent cited by the Examiner deals with a different problem - the degradation of collagen fibers giving the appearance of loose, wrinkled skin. Applicants thus submit that the term "smoothing" in Claim 4 is consistent with the present specification and the mechanisms discussed therein. Applicants further note that the Examiner indicated in the personal interview on May 28, 2003, that this rejection would be withdrawn upon amending Claim 4 to clarify that the smoothing effect resulted from the loosening and/or relaxing of the skin tissue. Withdrawal of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 102(b)

Claims 1, 4, and 24-31 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Lee et al. (U.S. Patent No. 5,569,678). The Examiner argues that Lee et al. disclose a method for minimizing or preventing excessive scar tissue. The Examiner argues that Lee et al. disclose a loosening or relaxing of the skin and that the muscular decontraction and/or relaxation is inherently achieved by the administration of the composition of Lee et al. This rejection, to the extent that it applies to the claims as amended, is respectfully traversed.

In order to anticipate a claim under 35 U.S.C. § 102, a reference must disclose or suggest each and every element of the claimed invention. By the present amendment,

claim 1 has been amended to recite "a regime or regimen for causing contractile fiber decontraction or relaxation to loosen and/or relax cutaneous and/or subcutaneous skin."

Applicants respectfully submit that Lee et al. do not disclose or suggest each and every element of the presently claimed invention.

Lee et al. disclose the prevention or treatment of scar tissue, by using a calcium channel inhibitor that controls the molecular (collagen and proteoglycan secretion) and cellular (fibroblast synthesis and cell shape) aspects of the scarring process (cf. col. 4, lines 1-41). The consecutive change toward matrix degradation gives a softened and faded scar tissue; however, there is no mention of any action on contraction/relaxation mechanism nor any specific effects of "loosening and/or relaxing" skin tissue, the object of the presently claimed invention. The scar tissue of Lee et al. is damaged skin tissue with molecular and cellular specificities (col. 1 and col. 4: growth factors, over-secretion of proteins and collagen) that are not shared by normal skin tissue. Accordingly, there is no evidence that a calcium channel inhibitor would have the same effect on both of these tissue types.

Contractile fiber decontraction or relaxation is disclosed or suggested nowhere in the Lee *et al.* publication. Lee *et al.* cite the overproduction of protein and collagen as leading to excessive scarring or keloid formation. (Col. 4, lines 21-25). In contrast, mechanisms such as contractile fiber decontraction or relaxation underlie the loosening and/or relaxing of cutaneous or subcutaneous tissue in the presently claimed invention. Thus, the purpose of Lee *et al.* is to prevent molecular and/or cellular disorders due to injury rather than utilizing the mechanical process of contractile fiber decontraction or relaxation. The end results of Lee *et al.* described in Example 5 are a softening and fading of scars,

disappearance of scar contracture, reduction in scar size and shrinkage of scars. (Col. 12, lines 5-24). In particular, Applicants respectfully submit that the effects of a reduction in scar size and shrinkage of scars directly contrast with the claimed invention which achieves a loosening and/or relaxing effect on cutaneous and/or subcutaneous tissue.

Lee et al. disclose that calcium channel antagonists are able to regulate cell shape, in particular, fibroblast shape (col. 4, Lee et al.), and viability of the cell. However, Lee et al. do not disclose that these features correlate with "smoothing of the skin," which the present specification shows is a result of a regulation of the contraction/relaxation mechanism of the underlying contractile fibers in cutaneous and subcutaneous tissue. Applicants respectfully point out that the microrelief of the skin is defined by micro-depressions on the surface of the skin, generated by fiber contraction phenomena.

Additionally, Applicants respectfully point out that the existence of calcium channels inside cutaneous and subcutaneous skin tissue was not determined until 1999 as disclosed in the specification on page 6, lines 9-11. Thus, neither Lee *et al.* nor one skilled in the art could have envisioned that the presently claimed invention was even possible in 1994 when Lee *et al.* filed their application. Accordingly, one skilled in the art would not have been motivated to apply the calcium antagonists to non-scared tissue, *i.e.*, cutaneous and/or subcutaneous tissue in need of loosening and/or relaxation. Thus, the presently claimed invention is not disclosed or even suggested by Lee *et al.*

Applicants respectfully submit that the candidate subjects of the presently claimed invention and that of Lee et al. are different. The presently claimed invention is aimed at loosening and/or relaxing cutaneous and/or subcutaneous skin tissue via contractile fiber

decontraction or relaxation. Thus, the subject in need of such treatment is one who requires contractile fiber decontraction/relaxation to smooth the skin. The subject of Lee et al. does not require contractile fiber decontraction/relaxation, but rather is afflicted with scars and requires the modulation of collagen biosynthesis. Accordingly, the subject populations of the presently claimed invention and Lee et al. are not the same. Therefore, Lee et al. cannot anticipate the presently claimed invention. One practicing the methods disclosed by Lee would not be practicing the presently claimed invention.

Withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 32 and 33 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Lee et al. in view of Perricone (U.S. Patent No. 5,965,618) or Lew (abstract, 1995). The Examiner argues that Perricone discloses a scar tissue treatment using lipoic acid and alpha hydroxy acid to enhance scar tissue reduction. Lew allegedly discloses a retinoid as an compound effective in wound healing and scar prevention. This rejection is respectfully traversed.

Applicants have demonstrated above the deficiencies of Lee et al. Namely, Lee et al. fail to disclose or suggest a regime or regimen for loosening or relaxing skin tissue by causing contractile fiber decontraction or relaxation and target different candidate subjects than the presently claimed invention. Perricone and Lew do not remedy this deficiency. Perricone discloses the use of lipoic acid for the treatment of scar tissue. Hydroxyacids are cited as additives. Lew discloses that a retinoic acid is able to modulate *in vitro* the

contraction of collagen gel via changes in the amount of actin and fibronectin receptor, and therefore could be used in the prevention of scar tissue in wound healing. Accordingly, neither Perricone nor Lew suggest the use of a calcium channel inhibitor to cause contractile fiber decontraction or relaxation to loosen and/or relax skin tissue, which is required by the presently claimed invention. Applicants respectfully submit that Perricone and Lew in combination with Lee et al. do not render the presently claimed invention obvious. Withdrawal of this rejection is respectfully requested.

Rejections Under the Judicially Created Doctrine of Obviousness-Type Double Patenting

Claims 1, 4, and 24-31 stand rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-11 of U.S. Patent No. 6,344,461. This rejection is respectfully traversed.

Applicants respectfully submit that the presently claimed invention may be utilized in other applications other than the treatment of skin wrinkles and fine lines. For instance, claim 4 demonstrates that the claimed regime or regimen can be used for smoothing the skin. Thus, the presently claimed invention is not obvious based on the claims of the '461 patent and is sufficiently distinct.

Further, the Examiner and Applicants' undersigned representative agreed that this rejection would be withdrawn upon amending independent claim 1 and claim 4 as above. Specifically, claim 1 has been amended to clarify that the contractile fiber decontraction or relaxation loosens or relaxes the skin and claim 4 amended to clarify that the smoothing of

the skin results from this mechanism. Withdrawal of this rejection is respectfully requested.

Conclusions

From the foregoing, further and favorable consideration of the subject application in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

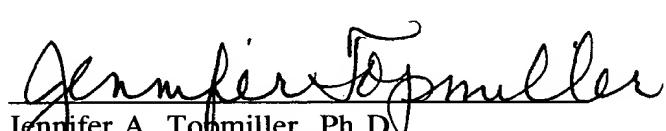
If there are any questions concerning this amendment or the application in general, the Examiner is requested to telephone Applicants' undersigned representative so that prosecution may be expedited.

Respectfully submitted,

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Attachment to Amendment dated June 12, 2003

Mark-up of Claims 1 and 4

1. (Twice Amended) A regime or regimen for causing contractile fiber decontraction or relaxation to loosen and or relax [loosening and/or relaxing] cutaneous and/or subcutaneous human skin tissue [via muscle decontraction or relaxation], comprising administering to a candidate subject in need of such regime or regimen, a thus-effective amount of at least one inhibitor of at least one calcium channel.

4. (Amended) The regime or regimen as defined by Claim 1, wherein said loosening and or relaxing of cutaneous and or subcutaneous human skin tissue smooths [for smoothing] the skin.